LASOP Resident/Fellow Symposium 2012

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Clinical History

- 62 year old female presented to ENT clinic with a right submandibular mass
- 4 years ago parotidectomy showed reactive lymphoid hyperplasia
- 2 years ago lacrimal gland biopsy showed reactive lymphoid hyperplasia
Current Physical Exam Findings

- Non-tender, firm right submandibular lymph nodes
- Bilateral cervical lymphadenopathy
- Left parotid enlargement
CBC Results

- WBC: 5.2 K/cumm
- Hgb: 13.4 g/dL
- Plt: 386 K/cumm

Differential:
- Segs: 45.3%
- Lymphs: 37.8%
- Monos: 10.8%
- Eos: 5.0%
- Basos: 1.1%
Imaging Studies
Submandibular Gland
Diagnosis??
IgG4 Related Disease
IgG4-Related Disease

• “Newly recognized fibroinflammatory condition characterized by tumefactive lesions, a dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells, storiform fibrosis, and, often but not always, elevated serum IgG4 concentrations”.

IgG4-Related Disease

• First reported in autoimmune pancreatitis

• Recognized as systemic condition in 2003, when extrapancreatic manifestations identified in patients with autoimmune pancreatitis.

Solitary or Multiorgan Involvement

- Biliary tree (Sclerosing Cholangitis)
- Salivary glands (Mikulicz’s Disease)
- Periorbital tissue (Sclerosing Dacryoadenitis)
- Soft tissue (Retroperitoneal Fibrosis)
- Lymph node
- Meninges
- Aorta
- Breast
- Prostate
- Thyroid
- Pericardium
- Skin
- Lung
- Kidney
Lacrimal Gland Biopsy (2010)
Immunohistochemistry

CD 138

IgG

IgG4
Parotidectomy (2008)
Immunohistochemistry

CD 138

IgG

IgG4
Epidemiology

- Male predominance; questionable
- Median age: 50 (range 12-83)
- Incidence: 2.63-10.2/million people (Japan)
- Sub-acute
- Often identified incidentally
Associated Laboratory Findings

- Elevated serum IgG and/or IgG4
- Elevated IgE
- Antinuclear Antibodies (ANA)
- Rheumatoid Factor
Additional Lab Results

- **ANA screen:** Pos
- **RF:** 74 IU/mL (< 14)
- **Immunoglobulins:**
  - IgG: 1073
  - IgM: 57
  - IgA: 65
  - IgE: 45

IgG subclass (mg/dL)
- IgG 1: 893
- IgG 2: 195
- IgG 3: 84
- IgG 4: 49.4*

*Normal in this case
Clinical Features

• Tumefactive lesions mimicking malignancy

• Allergic Disease
Allergic Disease and IgG4

- Common – 40%
  - Asthma
  - Chronic Sinusitis
  - Atopy
  - Eczema
  - Mild Eosinophilia
Diagnostic Criteria

• Histopathologic features

• Immunohistochemical features
Histopathologic Features

- Inflammatory infiltrate composed of mixture of T and B cells
- Stromal/vascular proliferation
- Polyclonal light chain expression
- Late phase of organ involvement has fewer plasma cells and more fibrosis
Histologic Patterns in Lymph Nodes

- Multicentric Castleman disease-like
- Follicular hyperplasia
- Interfollicular expansion
- Progressive transformation of germinal centers
- Inflammatory pseudotumor-like areas
Histologic Features in Lymph Nodes

- Dense lymphoplasmacytic infiltrate
- Perifollicular granulomas
- Mild-to-moderate eosinophil infiltrate
- Capsular and interfollicular fibrosis with storiform pattern
Histologic Features in Lymph Nodes

- Increase in intrafollicular plasma cells
- Increase in interfollicular plasma cells
  - Cytologically mature
  - Russell bodies and Mott cells
- Prominent Immunoblasts
Histologic Features in Exocrine Glands

- Dense lymphoplasmacytic infiltrate
- Obliterative phlebitis
- Mild-to-moderate eosinophil infiltrate
- Storiform fibrosis with parenchymal damage
Histologic Features in Exocrine Glands

- Infiltrate often surrounds ductal structures

- Obliteratorive phlebitis often present in pancreas and submandibular glands, less often in lacrimal glands and not seen in lymph nodes.
Immunohistochemical Diagnostic Criteria

• IgG4 plasma cells > 50 cells in a 40X high-power field AND

• > 40% of IgG-positive plasma cells positive for IgG4
Serum IgG4

• Elevated IgG4 serum level (> 135 mg/dl) is a helpful but nonspecific diagnostic marker

• Also seen in:
  – Pancreatic Adenocarcinoma
  – Primary Sclerosing Cholangitis
  – Inflammatory Bowel Disease
  – Hashimoto’s Thyroiditis
  – Atopic Dermatitis
Differential Diagnosis in Lymph Nodes

- Non-Hodgkin Lymphoma
- Follicular Hyperplasia
- Nonspecific Interfollicular Hyperplasia
- Progressive Transformation of Germinal Centers
Differential Diagnosis in Lymph Nodes

- Plasma Cell Castleman’s Disease
- Infectious Lymphadenitis
  - Luetic Lymphadenitis
- Autoimmune Lymphadenitis
  - Rheumatoid Lymphadenitis
Differential Diagnosis in Salivary Glands

- Chronic Sialadenitis
- Sjogren’s Syndrome
- Lymphoepithelial Sialadenitis
Treatment Options

- Surgical Excision
- Corticosteroids
- Azathioprine
- Mycophenolate mofetil
- Methotrexate
- Rituximab
Summary

• IgG4-related disease is a newly described clinicopathologic entity

• Diagnostic criteria and clinicopathologic manifestations continue to evolve

• Diagnosis is important due to marked steroid responsiveness in most cases
References